**Evaluation of lidocaine/ropivacaine combination for epidural anesthesia in goats**

Cecilia Omowumi Oguntoye and Faith Ifeoluwa Adewale

Department of Veterinary Surgery and Radiology, University of Ibadan, Ibadan, Nigeria

Author for correspondence: Cecilia Omowumi Oguntoye

Telephone no: +234 8055063671

Corresponding author Email address: wumcel06@yahoo.com

Department of Veterinary Surgery and Radiology, University of Ibadan, Ibadan, Nigeria

**ABSTRACT**

This study evaluated lidocaine/ropivacaine combination for epidural anesthesia by comparing the anesthetic indices and physiologic changes associated with epidural administration of lidocaine, ropivacaine and lidocaine- ropivacaine combination in goats. Using a prospective crossover study design, four male adult West African Dwarf goats received epidural injections of lidocaine (2 mg kg-1), ropivacaine (1 mg kg-1) and lidocaine- ropivacaine (1 mg kg-1; 0.5 mg kg-1) at two-week treatment intervals for drug wash out. Onset of analgesia was significantly longer (p ˂ 0.05) with lidocaine - ropivacaine (6.25 ± 2.22 minutes) than with ropivacaine (3.50 ±1.73 minutes) and lidocaine (3.00 ± 1.63 minutes). Duration of analgesia was significantly (p ˂ 0.05) longer with lidocaine - ropivacaine (168.50 ± 45.53 minutes) than with lidocaine (98.00 ± 26.65 minutes) but significantly shorter (p ˂ 0.05) than with ropivacaine (229.25 ± 33.54 minutes). Respective values for duration of recumbency and time to standing were intermediate with lidocaine - ropivacaine (137.00 ± 57.87; 200.50 ± 37.17minutes); longest with ropivacaine (167.00 ± 55.94; 281.25 ± 23.77 minutes) and shortest with lidocaine (80.75 ± 28.27; 130.50 ± 24.72 minutes) (p≤0.05). There were no significant differences (p ≥ 0.05) in physiological parameters temperature, heart and respiratory rates of goats following the three treatments. Epidural ropivacaine appears the best for long surgical procedures. The lidocaine-ropivacaine combination will be useful for procedures of moderate duration where a longer duration of analgesia than that produced by lidocaine alone is needed or where shorter recumbency period than possible with ropivacaine alone is desirable.

Keywords: epidural anesthesia, combination, goat, lidocaine, ropivacaine

Running title: Epidural anaesthesia in goats

# INTRODUCTION

In ruminants, general anesthesia and associated recumbency are often complicated by continuous salivation, ruminal tympany and regurgitation with the potential for aspiration into the lungs (Clarke *et al*., 2014); as a result, local or regional anesthesia is often employed in these species (Borer-Weir, 2014; Lin, 2014). Administration of drugs through the epidural route is a widely used regional anesthetic technique in human and veterinary patients (Campoy, 2004; Steagull *et al*., 2017), due to the route’s proximity to the spinal cord receptors involved in the modulation and transmission of the nociceptive signal (Steagull *et al*., 2017). Epidural block is produced by injection of a local anesthetic agent into the epidural space at the lumbosacral junction or at the sacro- coccygeal junction to provide analgesia and loss of motor function to allow surgery (Borer-Weir, 2014). Lidocaine hydrochloride is the most commonly used local anesthetic agent for this purpose in veterinary patients (Araujo *et al*., 2012). Lidocaine has a fast onset of action and provides excellent muscle relaxation but has a short duration of action and may require re-administration to complete a long surgical procedure (Campoy, 2004; Marongiu, 2012). Bupivacaine is a longer acting agent (6 - 8 h). However, it has a slower onset of action (40 minutes) and has potential for cardiotoxicity that is difficult to treat (Campoy, 2004; Leone, *et al*., 2008; Clarke *et al*., 2014). Ropivacaine is a new member of the amide class of local anesthetics, which recently gained entrance into the human medical practice. The drug is yet to be widely used in veterinary medicine, despite being considered a safer alternative to bupivacaine due to its lower toxicity and less arrhythmogenic effects on the central nervous and cardiovascular systems (Takenami *et al*., 2012; Kamble *et al*., 2016; Steagull *et al*., 2017). However, a few publications have compared ropivacaine and its combination with adjuvants in buffalo (Sekhar *et al*., 2020), and in cattle (Araujo *et al*., 2012; Kinjavdekar *et al*., 2015). In these studies, a longer onset of analgesia and shorter duration of analgesia were recorded in comparison with combinations with adjuvants (dexmedetomidine and clonidine) in buffalo (Sekhar *et al*., 2020) and in cattle (Araujo *et al*., 2012; Kinjavdekar *et al*., 2015). In goats, the sole use of ropivacaine in comparison with other drugs (Howell *et al*., 1990) and in varying doses (Kamble *et al*., 2016), produced a significantly shorter duration of analgesia when compared with bupivacaine alone and xylazine- ketamine combination.

An ideal local anesthetic agent should produce a fast onset and a long duration of analgesia without prolonged paralysis and toxic potentials (Lazar *et al*., 2014; Howell *et al*., 1990). No single agent currently available for use in clinical practice combines all these properties. Consequently, there have been investigations into the effects of mixing local anesthetic agents in order to meet these requirements (Seow *et al*., 1982; Powel *et al*., 2019). A 50:50 mixture of lidocaine-bupivacaine for epidural administration has been reported in humans, dogs, goats, cats and rats (Seow *et al*., 1982; Magee *et al*., 1983; Cruz *et al*., 1997; Lawal and Adetunji, 2009; Oguntoye and Adetunji, 2009; Dehkordi *et al*., 2012; Powel *et al*., 2019). Recently lidocaine-ropivacaine combination was evaluated for brachial plexus block in humans (Lazar *et al*., 2014). There is however a dearth of information in literature on the effects of epidural administration of lidocaine-ropivaciane combination in West African Dwarf (WAD) goats. This study therefore evaluated the anesthetic and physiological effects of lumbosacral epidural injection of a mixture of lidocaine-ropivacaine and compared with those of lidocaine or ropivacaine alone in WAD goats.

# MATERIALS AND METHODS

## Animals

Four healthy, adult WAD goats (bucks), 8.2 kg ± 1.0 (Means± SD) were used for the study. They were obtained from a goat market in Ibadan, Nigeria, housed together in a spacious, well-ventilated pen and fed with concentrates and cassava peels. Water was provided free choice in the pen.

## Drugs

The drugs used were Lidocaine hydrochloride (Glocain®, Vital Health Care PVT Ltd, India) supplied as 20mg per ml of colourless, aqueous solution with adrenaline in a 20-ml multidose vial and Ropivacaine hydrochloride (MACKLIN® Ropivacaine hydrochloride; Shanghai Macklin Biochemical Co. Ltd, China) supplied as a 1g white crystalline powder. This was reconstituted with water for injection at 0.75% (7.5mg/ml).

## Experimental Design

The goats were randomly subjected to three sets of trials carried out at two- week intervals in a simple crossover design. The trials consisted of epidural administration of Lidocaine hydrochloride (2mg/kg; LID group), Ropivacaine hydrochloride (1mg/kg; ROP group) and a combination of Lidocaine - Ropivacaine (1mg/kg and 0.5mg/kg respectively; LRM group). Heart rate (HR), respiratory rate (RR) and rectal temperature (RT in °C) were measured immediately after epidural injections and subsequently at 10 minutes’ intervals over a 2-hour period.

## Lumbosacral epidural Procedure

The goats were manually restrained on sternal recumbency with their fore limbs extended cranially. The spine of the seventh lumbar vertebrae, wings of the ilium, and the crest of the sacrum were palpated and the lumbosacral space identified. The area was shaved and aseptically prepared. A skin bleb was made at the lumbosacral junction with 1ml lidocaine to enhance a painless epidural puncture. An 18-gauge x 3.25 cm hypodermic needle was placed and correct needle placement was confirmed by loss of resistance to pressure on injection of 1ml of air. The appropriate local anesthetic agent was then injected into the epidural space. The development of motor and sensory blockade was assessed by loss of motor function resulting in the goats’ inability to stand on its hind limbs. Analgesia was assessed by response or lack of response to serial skin pin pricks of the areas caudal to the umbilicus (flank and ventral abdomen caudal, perineum and hind limbs) as previously described (Dehkordi *et al*., 2012).

## Calculations

2.5.1. Time to recumbency: This was defined as the time interval (in minutes) between epidural injection of anesthetic solution to paralysis of the goat’s hind limbs.

2.5.2. Time to onset of analgesia

Time to onset of analgesia wascalculated as the time interval (in minutes) between epidural injection of anesthetic solution and loss of reflex response to serial skin pin pricks of areas caudal to the umbilicus.

2.5.3. Duration of analgesia

The duration of analgesia was defined as the time interval (in minutes) between loss and return of response to serial skin pricks.

2.5.4. Duration of recumbency

The duration of recumbency (in minutes) was defined as the time interval between onset of paralysis of the goat’s hind limbs to first attempt to move the limbs.

2.5.5. Time to standing

The time to standing was recorded as the time interval (in minutes) betweenthe paralysis of the goat’s hind limbs to goat’s ability to walk.

## Measurements of physiologic variables

Respiratory rate in breaths/minute was determined by visual observation of chest movement, HR was measured in beats/minute with the aid of a precordial stethoscope and RT was determined using a mercury-in-glass clinical thermometer and measured in degrees centigrade (˚C).

## Statistical Analysis

Data was expressed as Means ± SD, and were compared using the one -way analysis of variance (ANOVA) at 5 percent confident limit.

# RESULTS

**3.1 Observations**

The mixture of lidocaine and ropivacaine was miscible with evidence of no precipitate formation. Following drugs administration, neural blockade was achieved in all the experimental goats evident by hind limb paralysis and loss of pain sensation.

**3.2 Anesthetic Indices**:

The anesthetic indices of the goats are shown on Table 1. The time to recumbency coincided with the onset of analgesia following each treatment (Table 1). The onset of analgesia was significantly longer (p˂0.05) with LRM (6.25 ± 2.22 minutes) than with ROP (3.50 ±1.73 minutes) and LID (3.00 ± 1.63 minutes) alone. The duration of analgesia was significantly longer with LRM (168.50 ± 45.53 minutes) than with LID (98.00 ± 26.65 minutes) but significantly shorter than with ROP (229.25 ± 33.54 minutes). The respective values for duration of recumbency and time to stand were significant at p < 0.05 and were intermediate with LRM (137.00 ± 57.87; 200.50 ± 37.17 minutes); longest with ROP (167.00 ± 55.94; 281.25 ± 23.77 minutes) and shortest with LID (80.75 ± 28.27; 130.50 ± 24.72 minutes).

Table 1: Anesthetic indices of goats following epidural administration of lidocaine, ropivacaine and lidocaine-ropivacaine

|  |  |  |  |
| --- | --- | --- | --- |
| Treatment groups  Time (min) | Ropivacaine  Mean+SD | Lignocaine  Mean+SD | Ropivacaine/Lignocaine Mean+SD |
| Onset of Action | 3.50+1.73 | 3.00+1.63 | 6.25+2.22\* |
| Onset of Analgesia | 3.50+1.73 | 3.00+1.63 | 6.25+2.22\* |
| Duration Analgesia | 229.25+33.54 | 98.00+26.65 | 168.50+45.53\* |
| Duration Recum | 167.00+55.94 | 80.75+28.27 | 137.00+57.87\* |
| Time to Standing | 281.25+23.77 | 130.50+24.72 | 200.50+37.17\* |

\*p<0.05

**3.3 Physiological variables:**

3.3.1 Heart rate

Ten minutes after administration of the drugs, there was a non- significant increase in HR with LID; decrease with ROP but increase and later slight decrease with LRM around the 80th minute. Overall, the HR values of the goats fell within normal range for LID and LRM (70 -94 beats/ minute) (Matthews, 1999; Smith, 2019) but a level of non-significant bradycardia with ROP (Fig. 1).

3.3.2 Respiratory rate

There were non-significant fluctuations in the respiratory rates with the three drugs but the values fell within normal physiological range for goats (Fig. 2).

3.3.3 Rectal temperature:

There was generally non-significantly higher rectal temperature with LID than with both ROP and LRM. (Fig. 3). Overall, rectal temperature values fell within normal range of 39 - 43°C quoted for goats (Smith, 2019).

Fig 1: Heart rate responses of goats to epidural injections of lidocaine, ropivacaine and lidocaine-ropivacaine (\*p<0.05).

Fig 2: Respiratory rate responses of goats to epidural injections of lidocaine, ropivacaine and lidocaine-ropivacaine combination.

Fig 3: Rectal temperature responses of goats to epidural injections of lidocaine, ropivacaine and lidocaine-ropivacaine.

# DISCUSSION

The results of this study showed that epidural lidocaine -ropivacaine produced the longest onset of action but intermediate duration of analgesia and recumbency. The lidocaine-ropivacaine combination in this study was intended to evaluate a possible synergism that could be of value in clinical practice considering the characteristics of both amides without undermining safety. Combinations of local anesthetics have been used to produce epidural anesthesia for possible advantages over single drugs (Martin-Flores, 2013). The three treatments (ROP, LID and RLM) produced hind limb paralysis and caudal analgesia of regions distal to the umbilicus (flank, perineum, inguinal. thigh and tail) in all the goats.

The onset of action for the three drugs in this study was LID ˂ ROP ˂ RLM. RLM produced a longer onset of action than ROP alone contrary to expectation. However, it has been postulated that since the pKa of mixtures of local anesthetics are not known, onset of action may not be predictable (Martin-Flores, 2013). The duration of analgesia with LRM in this study was intermediate (LID ˂ RLM ˂ ROP). Similar results have been obtained in studies that evaluated the effects of lidocaine-bupivacaine in which duration of analgesia of lidocaine - bupivacaine was also intermediate (Zand *et al*., 2004). One hypothesis concerning this observation is possibility of competition of local anesthetics for their receptors when used simultaneously so revealing shorter duration of action of the local anesthetic with more rapid onset of action (Zand *et al*., 2004).

Although there were undulations in the physiological values of the goats following the three treatments, the mean values for RR and RT (Figs 2 and 3) were within safety limits **(**10-30 breaths/min and 39 to 40 ºC) in goats (Smith, 2019). Mean values of HR (Fig 1) with LID and LRM were within physiological limits. Ropivacaine produced a level of bradycardia with some heart rate values (Fig 1) less the values of 70-94 beats/min acceptable in goats (Smith, 2019; Martin- Flores, 2013). Similar observation was reported by Singh *et al*., (2015) following epidural administration of ropivacaine in goats. The goats however all recovered uneventfully.

# CONCLUSIONS

In conclusion, epidural ropivacaine appears the best for long surgical procedures. However, the combination is safe and useful for procedures of moderate duration where a longer duration of analgesia than that produced by lidocaine alone is needed or where shorter recumbency period than possible with ropivacaine alone is desirable.

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